Chemical profiling of drug sensitivity in *P. falciparum* malarial strains.
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Although we have made great progress in fighting malaria, including the sequencing of several Plasmodium genomes and collection of genotypic data, we know very little about how variation in drug resistance between parasite strains relates to genomic differences. We propose to profile over 100 P. *falciparum* field strains for sensitivity to almost 3,000 approved drugs using an assay that measures parasite proliferation in red blood cells. This work will lead to a database of malaria chemical phenotypes that, in combination with genome-wide single nucleotide polymorphism (SNP) and microsatellite data, will be used to map genes that contribute to differential responses to particular drugs. This work will identify genes involved in malarial drug resistance, map the geographic distribution of drug responses, dissect the metabolic pathways of malaria parasites, and potentially discover new anti-malarial drugs or drug combinations.

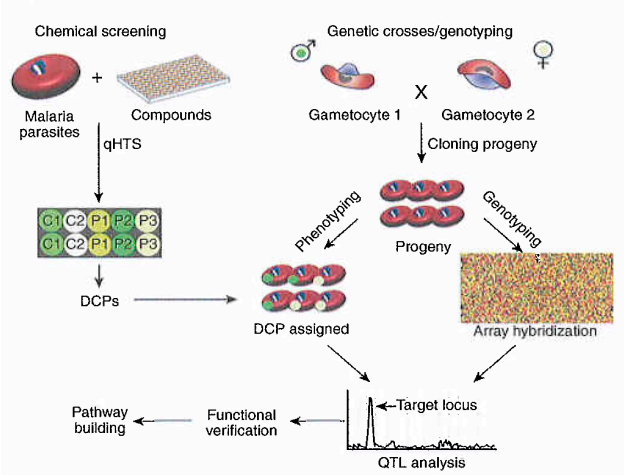

Figure 1 A chemical genomic strategy for studying gene function in malaria parasites. qHTS of parasites against compounds in titration-response fashion identifies a large number of DCPs. Target genes associated with these DCPs can be identified using quantitative trait loci analysis after genotyping progeny from genetic crosses or field isolates. Gene functions can be deduced from classes of compounds that target specific biologic pathways. The green circles represent differential parasite responses to chemicals. C1 and C2 represent negative and positive controls, and P1–P3 represent responses from three parasites. Gametocytes are the sexual stage of the malaria parasite that can be cultured *in vitro*, and a genetic cross is started by feeding a mixture of gametocytes from two different parasites to mosquitoes.